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OBSERVATIONS ON THE PRESENCE OF THE MENINGOCOCCUS IN THE BLOOD

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With the growth of our knowledge of epidemic meningitis, the presence of the causative organism in the blood stream has received increasing attention. From an essentially meningitic affection, the disease has come to be viewed by many as a primary sepsis with secondary invasion of the meninges as the usual — but not the necessary — accompaniment. Strong evidence in support of this view has been brought recently by the work of Baeslack¹ and Herrick² and their co-workers. The following observations, made at Camp Beauregard during the epidemic in Jan. and Feb., 1918, are of interest in this connection.

It was considered of practical importance in the study of the epidemiology of the disease at this camp to ascertain whether the abortive type of case was of common occurrence. The carrier theory was not altogether satisfactory in tracing the development of the epidemic. The term "abortive type" is used in this relation for those cases of meningococcus infection in which the organism invades the blood stream for a short time but is overcome by natural immunity before secure localization in the meninges is effected. Such cases might easily go unrecognized — passing as "grippe" or "influenza" — and if of frequent occurrence might play an important rôle in the spread of the disease.

At the suggestion of Major George Draper, efforts were made to determine this point. This entailed close watch over the admissions to the base hospital and daily visits to the regimental infirmaries to discover cases that might fall into such a group. Particular attention was paid to patients who were thought to have influenza, or regarded as "meningitis suspects" or "meningitis contacts." An examination was made for evidence suggesting a meningococcus infection, that is, petechial eruption, fever, malaise, headache, etc., without an obvious

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¹ Jour. Am. Med. Assn., 1918, 70, p. 684.

² Arch. Int. Med., 1918, 21, p. 541.

explanation. If the clinical picture was thought suggestive, a blood culture was made.

TECHNIC

The technic was similar to that advocated by Baeslack,¹ namely, 10-20 c c of blood were withdrawn and introduced into a flask (or small grape-juice bottle) containing 100 c c of a 1 per cent. glucose, salt-free broth which was usually enriched by adding a small amount of sheep serum water. Special care was taken to adjust the reaction of the medium so that it was neutral or just slightly acid after autoclaving. At first the titration was carried out with phenolsulphonephthalein as an indicator and the first faint trace of pink, permanent after boiling, as the neutral point. This was found unsatisfactory, and later use was made of solutions of phosphate mixtures of known hydrogen ion concentration as standards, to determine the hydrogen ion concentration of the medium more exactly with cresol purple as an indicator. An especial effort was made to keep the flask approximately at body temperature from the time the blood was withdrawn until it had been placed in the incubator. For this purpose, a fireless cooker heated by hot water bottles was used, when the cultures were made at a distance from the base hospital.

At the end of 48 hours and again at the end of 72, 2 c c of the culture were pipetted off from just above the blood, which had settled out in the bottom of the flask, and poured over the surface of laked sheep blood dextrose agar plates. After being allowed to stand for an hour the plates were tilted to drain off the moisture. They were examined in 18-24 hours for the characteristic colonies. The original flask was kept for 5 days, and if it showed no suspicious turbidity, and the blood-agar plates had proved negative, the culture was declared sterile.

RESULTS

Of a large number of patients examined, 27 were selected as clinically suggestive of possible meningococcus infection. None of these showed petechiae. All fell in to the group of fever, malaise, headache, etc., of unexplained origin, many of them being persons who had been in close contact with actual cases of epidemic meningitis.

In these 27 cases blood cultures were made. The results were entirely negative. In no case could the meningococcus be demonstrated.

As a result of this work, it was inferred that the "abortive type" of meningococcus infection, as defined above, was not of frequent occurrence, if, indeed, it occurred at all in the epidemic at Camp Beauregard. It certainly could not be considered a factor in the spread of the disease.

During the course of this investigation two cases of epidemic meningitis were encountered which illustrate very beautifully how brief and relatively unimportant the blood stream invasion may be in the one, as contrasted with the paramount importance which it may assume in the other, certainly more rare, type of case. Facts bearing on this point are of so much practical importance in determining the relative

value of the intraspinal and the intravenous mode of administering antimeningococcus serum that it is thought worth while to report the histories.

CASE 1.—The patient was admitted to his regimental infirmary late in the afternoon of Feb. 13 with headache, malaise and fever. The following morning about 10 o'clock when he was examined he had no meningeal symptoms and no petechiae, and might well have passed as a case of "grippe." A blood culture was made at this time, and proved positive for the meningococcus.

Subsequently the symptoms became exaggerated, and he began to vomit and grow dull mentally. He was transported to the base hospital as a meningitis suspect. By 2 o'clock of the same day his meningeal symptoms had become pronounced and a few petechiae were visible over the abdomen. A lumbar puncture was made and the fluid obtained was turbid and contained meningococci. Antimeningococcus serum was given intraspinally. One hour later, that is 5 hours after the first and positive blood culture, a second blood culture was taken with exactly the same technic and under more favorable conditions, since the case was now in the base hospital, and it proved to be entirely negative for the meningococcus.

The meningococcus obtained from the first blood culture and from the spinal fluid proved to be a normal strain. It agglutinated slightly up to a dilution of 1:100 with para-normal serum, but very well up to a dilution of 1:400 with the normal and polyvalent serum.

The further history of this case was as follows: He was given 3 intravenous treatments on successive days with intensive intraspinal treatment over a longer period. He responded well and on the 5th day he was greatly improved, temperature, pulse, and respiration had reached normal, and the spinal fluid was clear. On the following day he suddenly became comatose with stertorous breathing and died in a few hours. At necropsy the meninges were found to be entirely clear of exudate, but there was a large hemorrhage over the base of the brain apparently originating from the basilar artery or one of its branches.

In this case, there was apparently a transient meningococcus invasion of the blood stream—a meningococcemia. The organism disappeared from the blood stream within 24 hours, localizing in the tissue of predilection—the meninges. Here it was attacked successfully by the intraspinal administration of serum supplemented, perhaps unnecessarily, by intravenous injections. Death occurred from a vascular accident, the exact cause of which was not apparent.

In direct contrast to the foregoing is the second case:

CASE 2.—The patient began to have chilly sensations and feel sick while drilling on the afternoon of Jan. 11. The following morning he reported at sick call and was taken to the regimental infirmary. There he remained 4 days, passing as a case of "influenza." On Jan. 15 he was transferred to the base hospital because he did not improve. At this time he did not seem particularly sick, but because he vomited once or twice and had just a suggestion of a stiff neck, a lumbar puncture was made and a slightly turbid fluid obtained. The patient was immediately transferred to the meningitis ward where specific treatment was instituted by both the intravenous and intraspinal routes. The

details of his treatment are shown in Table 1. The spinal fluid quickly became clear, but the fever persisted and there was nausea, headache, vague bodily pains, restlessness and general weakness. He was given a second series of intraspinal treatments with slight temporary improvement. On Feb. 8, 3 weeks after the onset of his illness, a lumbar puncture again showed the spinal fluid clear, not increased in pressure, and free from organisms—although the same clinical symptoms persisted. The coexistence of another disease was suspected, but no proof could be brought by physical examination or laboratory aids.

TABLE 1
DETAILS OF TREATMENT FOLLOWED IN CASE 2

Date	Maximum Temperature	Intra-spinal Serum, c c	Intra-venous Serum, c c	Remarks
Jan. 17	101.8	25	..	Fluid cloudy; organisms not seen, but grown in culture
18	102.8	30	60	
19	101.6	30	60	
20	103.4	30	60	
21	103.8	—	..	Fluid clear; no organisms; few pus cells
22	99.0	30	..	
30	101.3	30	..	Fluid clear; few pus cells
31	100.8	—	..	
Feb. 1	98.0	30	..	
2	96.6	—	..	
3	98.0	30	..	Fluid clear; slight coagulum
8	101.6	—	..	Fluid clear; few cells; 5% mononuclears; leukocytes, 20,400
14	103.2	Leukocytes, 17,000; 77% polymorphonuclears
19	98.0	Blood culture No. 1, positive
21	100.8	Blood culture No. 2, positive; patient desensitized to serum
22	102.8	..	10	
23	102.4	..	40	
23	102.4	..	40	Leukocytes, 18,000
24	104.2	..	60	Blood culture No. 3, negative
25	104.6	..	40	Blood culture No. 4, positive
26	99.8	..	60	
27	104.0	..	—	
28	105.4	..	60	Blood culture No. 5, negative
Mch. 1	104.6	..	60	Leukocytes, 16,800
2	102.2	..	60	
3	102.2	..	60	
9	99.6	Blood culture No. 6, negative
15	100.9	Blood culture No. 7, negative
17	97.8	Leukocytes, 8,600

On Feb. 17, 4 weeks after the onset of his illness, it was noted that the patient had an eruption. It consisted of red macules or maculopapules, varying in size from a pea to a dime, some of them definitely nodular. They were distributed chiefly over the extremities, especially over the dorsum of the hands and feet with a few over the chest. They did not disappear on blanching the area; did not itch and were not painful. The eruption immediately suggested a hematogenous infection of some description, the nodules being somewhat similar to those seen in staphylococcus septicemia.

On Feb. 19 a blood culture was made and the meningococcus recovered. Two days later this was confirmed by a second positive culture. After the patient had been desensitized to horse serum, the intravenous injection of anti-meningococcus serum was begun. The dosage and intervals are shown in the table. In all 490 c c were given in a period of 10 days. The patient had violent reactions after the first 4 injections of this series in spite of his desensitizing

doses, but thereafter had very little trouble. After the sixth injection the blood culture became negative and remained so. The patient improved steadily and the temperature gradually declined until it reached normal. April 17 he was apparently well.

The meningococcus recovered in the blood cultures was of the normal type. It agglutinated up to 1:400 with normal and polyvalent serums. With the patient's own serum, taken before treatment was instituted on Feb. 21, it agglutinated up to 1:20. With a specimen taken after 4 intravenous treatments it agglutinated up to 1:40, showing some increase in the agglutinin content of the blood, presumably as a result of the intravenous injections.

In this second case, then, we were dealing with a true meningococcus sepsis. The meningitis was transitory and yielded quickly to intraspinal treatment. The organism, however, was able to survive and perhaps to multiply in the blood stream. No focus of distribution could be demonstrated. Nasopharyngeal swabs were repeatedly negative. There was never any indication of chronic infection in the upper respiratory tract, and the heart was entirely normal. The patient recovered fully after persistent intravenous injection of antimeningococcus serum.

Such cases of meningococcus sepsis as this are probably quite rare. That a transient meningococcemia is far more frequent is indicated by the fact that positive blood cultures are seldom obtained late in the disease, and by the technic of blood culture itself, namely, the necessity of using large quantities of blood in a large amount of broth. Indeed, in the light of our present knowledge, it must be admitted that there may be many cases in which the organism never gains a secure foothold in the blood stream, but localizes directly in the meninges. The question of the mode of invasion from the posterior nasopharynx is still an open one. Each case should be considered a problem in itself and the treatment directed as the particular needs of that case indicate.

CONCLUSIONS

During the epidemic at Camp Beauregard in February, 1918, 27 blood cultures done on patients suspected of being cases of abortive meningococcus infection were negative.

In this epidemic the abortive meningococcus infection was not a considerable factor in the epidemiology of the disease.

A case of meningococcus infection is reported in which the blood stream invasion was transient and the organism quickly localized in the meninges where it yielded to the intraspinal injection of serum.

A case of meningococcus septicemia with transient meningeal involvement is reported with recovery only after the injection of large amounts of antimeningococcus serum intravenously.